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(54) Title: USE OF (4-ALKYLPIPERAZINYL) (PHENYL) METHANONES IN THE TREATMENT OF ALZHEIMER'S DISEASE

(57) Abstract: The invention provides a therapeutic method for treating at least one symptom of Alzheimer's disease in a mammal, such as a human, wherein the toxicity of a pathogen of β amyloid peptide mammalian cells is implicated and inhibition of the subsequently-induced pathological pathways is desired comprising administering to a mammal in need of such therapy, an effective amount of a benzoylpiperazine derivative, including pharmaceutically acceptable salts thereof.

INTERNATIONAL SEARCH REPORT

International Application No
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A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 A61K31/495 A61P25/28 C07D295/18

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 A61K C07D A61P

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, BIOSIS, WPI Data, CHEM ABS Data, BEILSTEIN Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P, X, L	<p>WO 2004/108666 A (SAMARITAN PHARMACEUTICALS; GEORGETOWN UNIVERSITY; LECANU, LAURENT; GRE) 16 December 2004 (2004-12-16) page 5, lines 21-23; compound SP008 figure 1; compound SP016</p> <p>-----</p> <p style="text-align: center;">-/--</p>	1-27

Further documents are listed in the continuation of box C.

Patent family members are listed in annex.

° Special categories of cited documents :

- "A" document defining the general state of the art which is not considered to be of particular relevance
- "E" earlier document but published on or after the international filing date
- "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- "O" document referring to an oral disclosure, use, exhibition or other means
- "P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search

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INTERNATIONAL SEARCH REPORT

International Application No

PCT/US2005/012028

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P, X	LECANU L ET AL: "Identification, design, synthesis, and pharmacological activity of (4-ethyl-piperazin-1-yl)-phenylmethanone derivatives with neuroprotective properties against beta-amyloid-induced toxicity" NEUROPHARMACOLOGY, PERGAMON PRESS, OXFORD, GB, vol. 49, no. 1, July 2005 (2005-07), pages 86-96, XP004963513 ISSN: 0028-3908 the whole document -----	1-27
P, X	WO 2004/035556 A (GLAXO GROUP LIMITED; ANCLIFF, RACHAEL; ELDRED, COLIN, DAVID; FOGDEN, Y) 29 April 2004 (2004-04-29) claim 7 examples 1-11, 32-47 -----	1-27
A	US 5 693 804 A (DEBERNARDIS ET AL) 2 December 1997 (1997-12-02) column 5, line 50 - column 6, line 31 -----	1-27
A	WO 01/07435 A (MERCK PATENT GMBH; BOETTCHER, HENNING; GREINER, HARTMUT; HARTING, JUER) 1 February 2001 (2001-02-01) claims -----	1-27
A	US 2004/034019 A1 (TOMLINSON RONALD ET AL) 19 February 2004 (2004-02-19) examples 56, 57 -----	1-27
X	DE 23 04 155 A1 (ICHTHYOL-GESELLSCHAFT CORDES, HERMANNI & CO, 2000 HAMBURG) 1 August 1974 (1974-08-01) claims 1, 7 table 1 examples -----	25
X	YUNG D K ET AL: "POTENTIAL ANTI ARRHYTHMIC AGENTS SYNTHESIS AND PHARMACOLOGICAL EVALUATION OF SOME PIPERAZINE AND ETHYLENEDIAMINE ANALOGS OF PROCAINAMIDE 1 N PROPYL-4-BENZOYL PIPERAZINE HYDRO CHLORIDE 1 N BUTYL-4-BENZOYL PIPERAZINE HYDRO CHLORIDE 1 N PROPYL-4-P-METHOXYBENZOYL PIPERAZINE HYDRO CHLORIDE 1 N PROPYL-4-P" JOURNAL OF PHARMACEUTICAL SCIENCES, vol. 57, no. 12, 1968, pages 2073-2080, XP009055767 ISSN: 0022-3549 table III -----	25

INTERNATIONAL SEARCH REPORT

International Application No

PCT/US2005/012028

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	FUKUSHI H ET AL: "SYNTHESIS AND PLATELET-ACTIVATING FACTOR (PAF)-ANTAGONISTIC ACTIVITIES OF 1,4-DISUBSTITUTED PIPERAZINE DERIVATIVES" CHEMICAL AND PHARMACEUTICAL BULLETIN, PHARMACEUTICAL SOCIETY OF JAPAN, TOKYO, JP, vol. 42, no. 3, March 1994 (1994-03), pages 541-550, XP001118308 ISSN: 0009-2363 compound 2B table 1; compounds 2A-2M -----	25
X	YOUNES-EL-HAGE S ET AL: "SYNTHESE ET ETUDE DE L'ACTIVITE ANTIDEPRESSIVE D'ARYL ET HETEROARYL CARBOXAMIDES DE LA BENZYLPIPERAZINE SYNTHESIS AND ANTIDEPRESSIVE ACTIVITY STUDY OF ARYL AND HETEROARYL CARBOXAMIDES OF BENZYLPIPERAZINE" ANNALES PHARMACEUTIQUES FRANCAISES, MASSON, PARIS, FR, vol. 58, no. 4, 2000, pages 254-259, XP008031993 ISSN: 0003-4509 table 1; compounds 1-14,23,24,27-42 -----	25
X	YOUNES S ET AL: "Synthesis and structure-activity relationships of novel arylalkyl 4-benzyl piperazine derivatives as sigma site selective ligands" EUROPEAN JOURNAL OF MEDICINAL CHEMISTRY, EDITIONS SCIENTIFIQUE ELSEVIER, PARIS, FR, vol. 35, no. 1, January 2000 (2000-01), pages 107-121, XP004350211 ISSN: 0223-5234 compound 5 -----	25
X	BAZIARD-MOUYSSET G ET AL: "Synthesis and structure-activity relationships of novel 2-amino alkyl chromones and related derivatives as sigma site-selective ligands" EUROPEAN JOURNAL OF MEDICINAL CHEMISTRY, EDITIONS SCIENTIFIQUE ELSEVIER, PARIS, FR, vol. 33, no. 5, June 1998 (1998-06), pages 339-347, XP004127366 ISSN: 0223-5234 table 1; compound 21 -----	25

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INTERNATIONAL SEARCH REPORT

International Application No

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	CARCELLER E ET AL: "(PYRIDYL CYANOMETHYL) PIPERAZINES AS ORALLY ACTIVE PAF ANTAGONISTS" JOURNAL OF MEDICINAL CHEMISTRY, AMERICAN CHEMICAL SOCIETY, WASHINGTON, US, vol. 35, no. 22, 1992, pages 4118-4134, XP002044180 ISSN: 0022-2623 table 1; compound 34 -----	25

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Box II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. Claims Nos.: because they relate to subject matter not required to be searched by this Authority, namely:
Although claims 1–24, 26 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
2. Claims Nos.: because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. Claims Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- The additional search fees were accompanied by the applicant's protest.
- No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

International Application No

PCT/US2005/012028

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